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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,307	01/11/2001	Sam J. Milstein	1946/1A483-US8	8759

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EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,307	MILSTEIN ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-37,50-73,87-110 and 112-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-37,50-73,87-110 and 112-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-24-04.* & 6-14-04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of IDS dated 7-27-04 and request for continued examination dated 6-30-04 is acknowledged.

Claims 13-37, 50-73, 87-110 and 112-189 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6-30-04 has been entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 13-37, 50-74 and 87-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 11-20 of U.S. Patent No. 6,071,538 ('538); claims 1-7 of U.S. 5,714,167 ('167); and 1-22 and 33-37 of U.S.

Patent No. 6, 348,207 ('207). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the claims of '538, '207 and '167 recite a method of delivering a biological agent comprising the same steps as that of instant claims i.e., a biologically active agent and a perturbant that reversibly transforms the active agent upon non-covalent binding with the active agent and together both the perturbant and the active agent form a supra molecular complex. The claims of the above patents recite the same perturbants as that claimed in the instant. The above patents fail to claim the instant routes of administration. However, absent evidence to the contrary it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the composition of the above patents containing an active agent and a perturbant that reversibly transform the active agent for administering via intranasal or sublingual or subcutaneous routes because the above patents recite the same mechanism of action of the perturbants in transporting the active agents, irrespective of the mode of administration i.e., the changed or altered confirmation of the active agents renders the active agent soluble to cross and penetrate the lipid bilayer membrane of the cells and resist enzymatic degradation. Accordingly, one of an ordinary skill in the art would have expected to transport the active agents of using the perturbants across other mucosal membranes such as those of nasal tissues or the mouth cavity.

2. Claims 13-37, 50-74 and 87-189 are directed to an invention not patentably distinct from claims 1-5 and 11-20 of commonly assigned US 6,071,538, claims 1-22 and 33-37 of U.S. Patent No. 6, 348,207 ('207) and claims 1-7 of U.S. 5,714,167 ('167). Specifically, the instant active agent transport systems containing a biologically active agent and a perturbant that

reversibly transforms the active agent, forming a non-covalent bonding with active agent is also described in the above patents.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US 6,071,538, 6,348,207 and 5,714,167 discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

3. Claims 13-37, 50-74 and 87-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over 6,017,538 (hereafter '538), 6,348,207 ('207) or 5,714,167 ('167).

Each of the above cited patents teach active agent transport systems containing biologically active agent that can exist in native or denatured or an intermediate conformational state which is exposed to a perturbant that is non-covalently bonded to the active agent. The

perturbant reversibly transforms the active agent to form a transportable supra molecular complex, and thus aids in the delivery of biologically active agent. The above patents teach the same classes of perturbants and active agents, which are claimed in the instant invention (see entire document); and that the transport system is capable of transporting active agents across mucus membranes such as gastro-intestinal mucosa. The above patents fail to teach the instant routes of administration. However, absent evidence to the contrary it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the composition of the above patents containing an active agent and a perturbant that reversibly transform the active agent for administering via intranasal or sublingual or subcutaneous routes because the above patents teach the same mechanism of action of the perturbants in transporting the active agents, irrespective of the mode of administration i.e., the changed or altered confirmation of the active agents renders the active agent soluble to cross and penetrate the lipid bilayer membrane of the cells and resist enzymatic degradation. Accordingly, one of an ordinary skill in the art would have expected to transport the active agents of using the perturbants across other mucosal membranes such as those of nasal tissues or the mouth cavity.

4. Claims 13-37, 50-74 and 87-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent No. 6,221,367. Although the conflicting claims are not identical, they are not patentably distinct from each other because the perturbant of the patented claims is a species the generic perturbants claimed in the instant invention.

Minor Informalities

5. Examiner notes that the word "reversibly" has been misspelled in the instant independent claims. It is suggested to applicants to correct the same.

Claim Rejections - 35 USC § 103

Claims 13-16, 18, 23-25, 27, 32, 50-53, 55, 60-62, 64, 69, 87-90, 92, 97-99, 101, 106 and 112-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,873,087 to Morishita et al (Morishita) in view of US 4,746,675 to Makino et al (Makino) or over Makino et al by itself.

Morishita teaches a preparation containing an absorption promoter and a medically active agent for promoting absorption through a gastrointestinal organ such as colon, rectum or through vagina. The absorption promoter substance of Morishita is an N-acyl amino acid or N-acyl peptide derivative, of formula I (col. 1, lines 5-10, col. 3, lines 13-15) and is obtained by the reaction of an acid (R-COOH) with an amino acid or peptide. The carboxylic acids and amino acids used for preparing N-acyl amino acids are described in col. 4 and 6 and include those described in the instant specification. Among the medically active agent, Morishita describes hormones, such as insulin, antibiotics etc (col. 5, lines 25-68). Morishita fails to specifically teach that the absorption promoter is non-covalently linked to the active agent or the molecular weight of the promoter. However, Morishita teaches the same components of the instant claims and accordingly the burden is shifted to applicants to show how the teachings of Morishita differ from the instant. Morishita does not specifically teach subcutaneous, intranasal or sublingual

delivery routes, instead teaches administration through rectum or vagina, which are lined by mucosal membranes.

Makino teaches external pharmaceutical composition for administering therapeutic agents via skin and mucosal membranes. The compositions of Makino comprise a pharmacologically active agent and a penetration enhancer, such as pyroglutamic acid derivatives (col. 4-8). The pyroglutamic acid derivatives shown by formula I (col. 4) of Makino read on the claimed acylated amino acid derivatives. Makino teaches a number of pharmaceutically active agents that can be administered using the above absorption enhancer (col. 10-12), which include those that are claimed in the instant application. Makino teaches that the penetration enhancers are capable of penetrating skin or mucosa and thus can enhance the absorption a wide range of (hydrophilic as well as hydrophobic) drugs; and also when administered by oral or injection route, the absorption enhancer prevents the drug from being degraded and maintain the effective blood levels over a long period of time (col. 3-4). The claimed routes of sublingual, intranasal involve mucosal administration. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ the pyroglutamic acid derivatives of Makino as absorption enhancers for a variety of pharmaceutical agents, administered by sublingual or intranasal or subcutaneous routes because Makino teaches that the compounds are extremely useful in delivering drugs orally, topically or mucosally without loosing the activity due to degradation or lack of transport through the mucosal or epidermal membranes. Similarly, it would have obvious for one of an ordinary skill in the art at the time of the instant invention to administer the absorption enhancers of Morishita via mucosal routes (sublingual or intranasal) or subcutaneous injection because Makino suggests that the amino acid derivatives are effective in

delivering a number of drugs administered by oral or injection or via skin or mucosal membrane, without loosing the activity of the drugs.

Response to Arguments

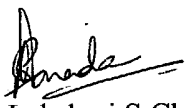
Applicant's arguments with respect to claims 13-37, 50-73, 87-110 and 112-189 have been considered but are moot in view of the new ground(s) of rejection.

With respect to the double patenting rejection over US patents 6,071,538 and US 6,621,367, applicants agreed to file a terminal disclaimer upon finding allowable subject matter. Accordingly, the rejection has been maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615
December 9, 2004